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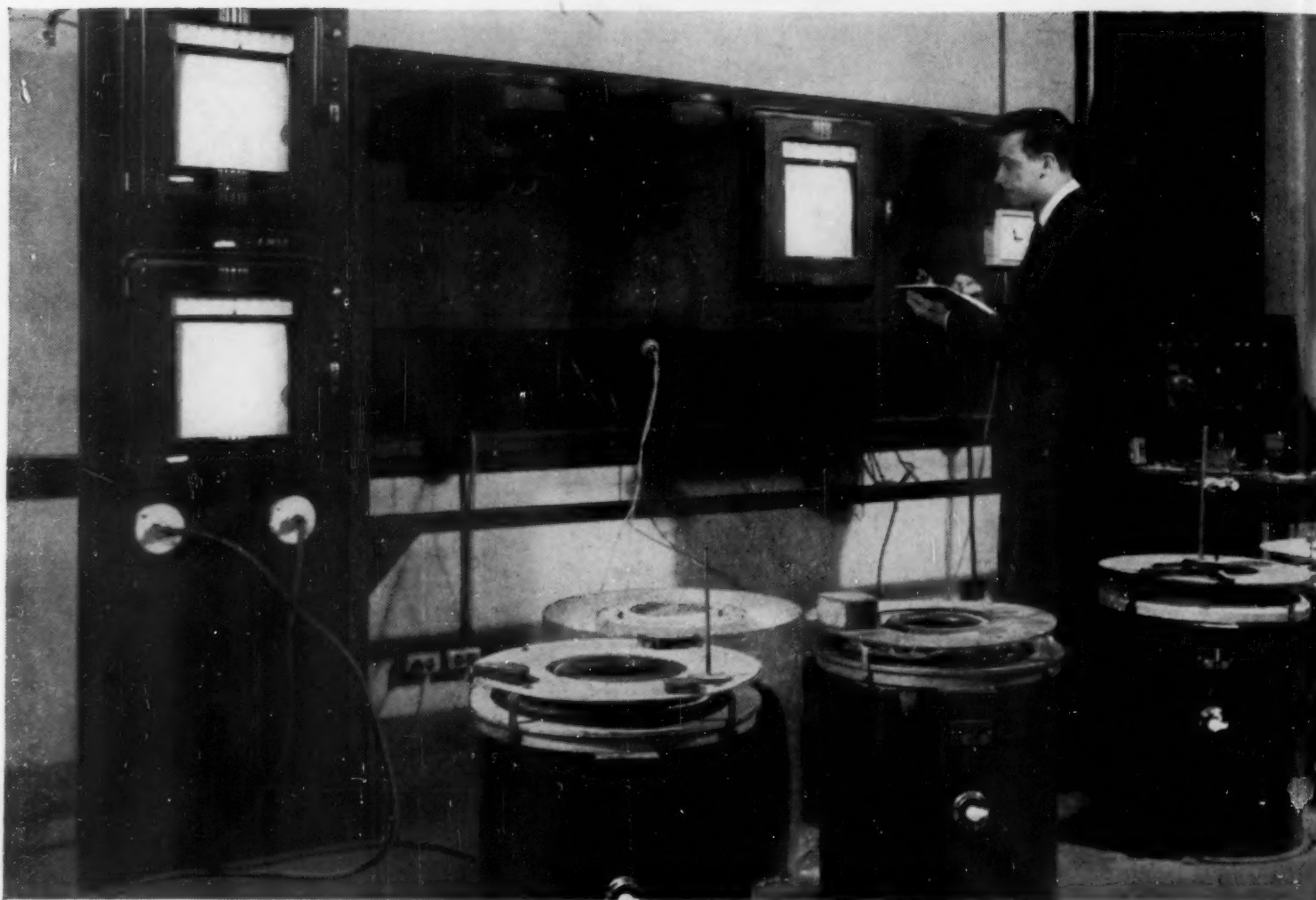
July 2, 1948

Science



Bausch & Lomb Science Scholarship Winners

(See page 6)



Metallurgist at University of Notre Dame transcribes temperature data from four-point Speedomax Recorder connected to furnaces in foreground. Experiment is part of

extensive studies of the grain growth which occurs during annealing of aluminum and aluminum alloys, described in AIME, Metals Tech., September, 1947.

Test Data from Four Electric Furnaces Recorded by Speedomax at Notre Dame

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The History and Ethics of the Use of Human Subjects in Medical Experiments

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ETHICS MEANS THINKING SINCERELY about rules for human conduct. Experimentation is a highly intellectual form of human activity. Hence, it is appropriate for experimenters to consider the ethics of their activities.

It should be recalled that all science or knowledge has two aspects, the descriptive and the experimental. Knowledge is obtained by describing and systematizing things and processes which are observed to occur in Nature and by designing and executing experiments to reveal the nature of the things and processes observed. Observation without experiment is quite sterile, as is witnessed by the type of culture of ancient civilizations. Observation and experimentation must be effectively combined to produce the culture characteristic of modern civilization. It has been through the experimental method of controlled or conditioned observation, and *only* through this method, that scientists have discovered and will continue to discover the most intimate secrets of Nature.

In the medical sciences, the only method which can clearly reveal and establish the cause, prevention, and treatment of disease is the method of controlled experimentation on animals and volunteer human subjects. Even after the therapy of a disease is discovered, its application to the patient remains in part experimental. Because of the physiological variations in the response of different patients to the same therapy, the therapy of disease is, and will always be, an experimental aspect of medicine.

We frequently forget to recall the fact that a patient is a voluntary experimental subject of the physician. The physician *practices* medicine today, and because the response of different patients to the same therapy will always vary to some extent, the physician will always *practice* medicine on his patient. No physician can honestly guarantee that he will cure a disease or that his treatment will not cause undesirable symptoms or temporary discomfort. In all cases except emergencies, the surgeon obtains the consent of

his patient or of a relative of the patient for operative treatment. Similarly, the internist has the consent of his patient or a relative before applying treatment.

The fact that the patient is always to some extent an experimental subject of the physician is the reason that Hippocrates formulated his famous Oath for Physicians. He realized that the scientific and technical philosophy of medicine could not survive without a sound moral philosophy. A society with a profession of medicine that has no moral philosophy is inconceivable.

THE RISE, FALL, AND RISE OF EXPERIMENTATION IN MEDICINE

Historically, Hippocrates (460-370 B.C.) is credited with the initiation of the descriptive science of medicine. Galen, who lived some 500 years later (131-201 A.D.), is similarly credited with the initiation of the experimental science of medicine, including the use of animals. Of course, there are indications of the performance of experiments on animals and man in the oldest literatures, but these will not be referred to here.

After Galen's death, the experimental method in medicine was not used throughout the Dark and most of the Middle Ages, or for 1,200 years. Then, Vesalius (1514-64 A.D.), by dissection of the human cadaver, which had previously been forbidden, and by animal experimentation, demonstrated certain inaccuracies in Galen's conception of the circulation of blood. This evidence of the renaissance from the barbarism and paganism of the Dark Ages was climaxed in 1628 by Harvey's "discovery of the circulation," which involved controlled observations on animals and man. Harvey used one of his subjects, a patient with an accidental exposure of the heart to the outside, in a demonstration before King Charles I, showing among other things, that the heart could be touched without causing pain. The great importance of controlled experiments was again demonstrated in 1798, when Jenner published his remarkable observations on vaccination against smallpox.

This paper was read at the Symposium on Human Pharmacological Experiments at the meeting of the Federation of American Societies for Experimental Biology held in Atlantic City, March 15-19, 1948.

RANDOM EXPERIMENTS ON MAN

Regardless of Harvey's demonstration of the great usefulness of controlled experiments on animals and man, the true significance of the philosophy and application of the method was not generally realized until the latter half of the 19th Century.

In the meantime, numerous physicians had seized the idea of experimentation but not the complete concept of controlled experimentation. So, throughout the 18th and 19th Centuries, numerous physicians performed more or less random experiments on themselves and their friends. Some examples will be cited. John Hunter in 1767 (3) confused medical knowledge by supposedly inoculating himself with gonorrhea from a patient. The inoculum produced both gonorrhea and syphilis, which convinced Hunter that the diseases were the same. Purkinje (7) in 1790 gave himself a large overdose of digitalis in order to study the changes in vision produced by the drug in his patients. The dose, which by modern standards would have killed 9 cats, produced in Purkinje cardiac pain and irregularity and caused him to vomit for a week. Early in the 19th Century, E. Hale (10), of Boston, enthusiastic about the intravenous administration of drugs, had himself injected intravenously with 0.5 ounce of castor oil and fortunately lived to describe his marked reaction. Tonery in 1830 demonstrated the capacity of charcoal to absorb alkaloids by taking an otherwise lethal dose of strychnine before the French Academy. Simpson introduced chloroform and Long, ether anesthesia, after testing them on themselves and friends. Morton (8), working more cautiously, tested ether on the family pets before trying it on himself.

After 1850, many instances are to be found in the medical literature in which potentially toxic chemicals and agents were first tried on man. In 1855 Christison chewed one-fourth of a Calabar bean (eserine), which resulted in symptoms so marked that his colleagues had to be called to treat him (11). Carbon tetrachloride was tried as an anesthetic in 1867 (9) in man when a few experiments on animals would have shown it to be unsuitable. Acetanilid was discovered in 1884 to have antipyretic properties when given to one of Prof. Kussmanka's assistants, whose body temperature fell alarmingly before he recovered (6). C. Oliver approached Prof. Schafer in 1894 (2) and reported that he had made extracts of all of the endocrine glands of the body and had injected them into his own son. Prof. Schafer changed the design of the experiment and was the first to demonstrate the pressor effect of epinephrine in dogs and cats. About 1900, Pierre Curie (4), when told that radium would produce skin burns, bandaged some radium bromide

onto his forearm, and allowed it to remain for several hours.

While these experiments may be a tribute to the enthusiasm and the bravery of these early medical scientists, they clearly show the limitations and dangers of uncontrolled self-experimentation.

ANTIVIVISECTION

Men such as Harvey, Jenner, Claude Bernard (1813-78), and Pasteur (1822-95) demonstrated clearly that controlled animal experimentation should be the basic method of research in the zoological sciences.

Despite the contributions of these and other benefactors of mankind, it is a strange fact that their animal experiments were attacked by a group of persons who called themselves Antivivisectionists. But it must be recalled that in the 18th and 19th Centuries chemists and physicists were attacked and maligned because they practiced the "black art" or constructed "devices of the devil." The attack on the latter subsided, however, during the last half of the 19th Century, whereas the attack of the Antivivisectionists grew in vehemence and burst into dramatic expression in Nazi Germany.

One of the first official acts of Hitler after he assumed power was to issue an edict rendering animal experimentation illegal. As a commentary on this action, the world now knows that the Nazis during the recent war used human beings without their consent as experimental subjects and without giving them the consideration which animals are given in scientific laboratories and veterinary hospitals. As another commentary on Hitler's edict, an entry in Goebbels' diary on October 15, 1925, reads: "I have learned to despise the human being from the bottom of my soul"; and another entry on August 17, 1926, reads: "The more I get to know the human species, the more I care for my dog."

Here in the words of Goebbels—the man whose false propaganda and racial views resulted in the most wanton torture and destruction of human beings in the history of the human race—we have the crux of the ethical questions regarding the use of animals and man as subjects in medical experiments. The questions are: Should one love animals more than human beings? Should one love disease more than health? Should one love ignorance more than knowledge of the living body?

ETHICS OF ANIMAL EXPERIMENTATION

Modern intelligent or literate people cannot seriously accept the view that animals, disease, and ignorance are preferable to human life, health, and

knowledge. In many ways, the existence of man stands in conflict with that of living plants and animals. The necessity of destroying and injuring living things is imposed on man, for it is by destroying plants and animals that man gets his food and clothing. In order to preserve his own existence, man must defend himself against any existence which would injure him.

How, then, can ethics be maintained in view of the necessities which confront man? Kant presumed that ethics are concerned only with the duty of man to man. A more universal and perhaps defensible view may be stated as follows: when one injures or takes the life of living things, one should be certain that it is necessary.

James Rowland Angell, formerly president of Yale University, in discussing the ethics of animal experimentation, has said in effect: If experimentation on living animals is justified by its results, the basic ethical issue is closed, provided the minimum of pain is caused, and the indirect effects are not such as to augment the spirit of cruelty.

John Dewey, professor of philosophy emeritus at Columbia University, on analyzing the ethics of animal experimentation, concluded: (a) "Scientific men are under definite obligation to experiment upon animals so far as that is the alternative to random and possibly harmful experimentation upon human beings, in so far as such experimentation is a means of saving human life and of increasing human vigor and efficiency. (b) The community at large is under definite obligations to see to it that physicians and scientific men are not needlessly hampered in carrying on the inquiries necessary for an adequate performance of their important social office of sustaining human life and vigor." Prof. Dewey remarks that "these things are so obvious that it almost seems necessary to apologize for mentioning them." *Yet, the acts of legislative assemblies in parts of the United States are such that dogs and cats are wantonly destroyed by so-called humane societies. If scientists did not oppose anti-vivisection legislation, all animal experimentation and even the production of vaccines for man and animals would be abolished within two years.*

This strange attitude on the part of antimicrobial groups, which is expressed in legislation restricting the procurement of animals, persists in the face of the fact that the vast majority of the American people contribute tens of millions of dollars yearly to research on cancer, heart disease, and infantile paralysis—research which, as we know, would be impossible without experimental animals; it persists regardless of the rules for animal experimentation adopted by the American Medical Association and all zoological groups of scientists.

Obviously, experiments may, and must, be per-

formed on lower animals if medical knowledge is to be advanced, and random, harmful, and unnecessary experimentation on man is to be avoided. The final test, however, must be made on human subjects. No one knows better than the biologist that caution must be exercised in applying to man the results of animal experiments; yet, every biologically literate person knows that the results of animal experiments have directed us to the greater amount of the most valuable part of our practical medical knowledge. There are also some medical experiments which can be performed only on man, because certain diseases are contracted only by man.

THE USE OF MEDICAL AND LAY SUBJECTS

It is a matter of common understanding that an individual may consent to undergo medical or surgical treatment, or other experimentation, for the good of his own body. A part of the body may be sacrificed to preserve the whole body. And, in desperate cases, more liberty is taken to apply remedies which have only a small possibility of accomplishing any good. It is also a matter of common understanding that an individual may justifiably permit a physical evil on himself for the good of another or for the good of humanity, with limitations which need not be mentioned here.

As it is well known, medical scientists, medical students, soldiers, sailors, and other volunteers have on many occasions served as subjects in medical experiments designed to advance human welfare. These have been conducted according to certain ethical principles in all countries of the world which have contributed to the prevention, cure, and control of disease and suffering. These principles, which have been in force by common understanding and practice, may be summarized as follows:

(I) Consent of the human subject has been obtained. All subjects have been volunteers in the absence of coercion in any form. Before volunteering, the subjects have been informed of the hazards, if any.

(II) The experiment to be performed has been based on the results of animal experimentation and on the knowledge of the natural history of the disease under study and has been so designed that the anticipated results will justify the performance of the experiment. It is the obligation of any investigator to study exhaustively a process or a substance in animals before undertaking hazardous experiments of a similar nature on human subjects. In addition, the experiment has been such as to yield results which are unobtainable by other methods of study and are necessary for the good of society.

(III) The experiment must be conducted (a) only

by scientifically qualified persons, (b) so as to avoid all unnecessary physical and mental suffering and injury, and (c) only after the results of adequate animal experimentation have eliminated any *a priori* reason to suspect that accidental death or disabling injury may occur. In such experiments as those of Walter Reed, in which it was demonstrated that the mosquito transmits yellow fever, medical scientists should serve, or should have served, as volunteers along with nonscientific personnel as evidence of the necessity of the experiment and their willingness to experience discomfort along with others for the sake of the solution of the problem.

These rules have been adopted in essence by the House of Delegates of the American Medical Association (14) and were introduced into the record of the Nuremberg Trials as representing generally accepted practice among medical scientists.

THE USE OF PRISONER VOLUNTEERS AS SUBJECTS

From time to time, prisoner volunteers have been used as subjects in medical experiments in the United States and abroad (15). A few examples under which they have been used in this country will be cited.

Col. R. P. Strong, later professor of tropical medicine at Harvard University, was apparently the first in the United States to use prisoners for medical experiments. With the permission of the Governor General of the Philippines, Col. Strong in 1904 used prisoners condemned to death who had volunteered to serve as subjects in experiments on the plague (12). Later he and B. C. Crowell (13) used prisoners, under similar conditions in the Philippines, as subjects in experiments on beriberi. The only reward given the prisoners during the course of the experiments consisted of gifts of tobacco. In 1914, Drs. Goldberger and Wheeler (5), of the U. S. Public Health Service, conducted experiments on pellagra on white male convicts in the State of Mississippi who volunteered for the experiments. The prisoners signed contracts promising to serve faithfully and were accordingly rewarded.

During the recent war, prisoners in both Federal and State Prisons, as is well known, were used in several different types of medical experiments, such as those involving malaria and the testing of drugs and blood plasma substitutes. More prisoners than were required volunteered in most prisons. Referring to prisoners who volunteered for medical research in a prison in New Jersey, Mr. Bixby, Deputy Commissioner of the Department of Institutions and Agencies of New Jersey said:

All prisoners who had participated in medical experiments were given certificates of merit, copies of which were put into their records and called to the special attention of the Court of Pardons or the Board of

Managers when parole was under consideration. Apparently no definite policy was ever formulated, and the participation in a medical experiment was considered only as one favorable factor in the whole case.

T. P. Sullivan, director of the Department of Public Safety of the State of Illinois, reports that essentially the same policy has been followed in the case of prisoners at Stateville who served in malaria experiments. When their cases came up for review, some reduction of sentence was allowed. In a letter to Mr. Sullivan, Mr. Ragen, warden at Stateville, stated: "Each will have to be treated as an individual case and consideration given accordingly."

In experiments conducted by the U. S. Public Health Service on prisoners in the Federal Correctional Institution at Seageville, Texas, the Under Secretary of War has ruled that volunteers (for medical experiments) will receive the same honorarium (\$100) and certificates of merit as the Atlanta participants but, in addition, will receive under the parole system some reduction of sentence for their participation.

In the consideration of the ethics involved in the case of prisoner volunteers, the generally accepted purposes of imprisonment should be reviewed. There are 5 such purposes (1): (1) *the punitive or retaliative*, historically the oldest purpose of imprisonment, which holds that revenge is the purpose of punishment; (2) *the expiative*, which holds that some sacrifice or atonement of penance by the wrongdoer is necessary and is best fulfilled by punishment; (3) *the exemplary or deterrent*, which attempts to prevent crime by the example of punishing persons who commit crime; (4) *the socio-protective*, or the wish to protect society from dangerous and vicious persons; and (5) *the reformative* which indicates that the purpose of imprisonment is to reform the prisoner.

The purpose of the parole system is also involved in the use of prisoner volunteers and should be reviewed. A reduction of sentence in prison is now recognized under the parole system "for the purpose of encouraging and rewarding good conduct and industry" and for "exceptional bravery or fidelity" in a good cause. The parole law is based on the presumption that the reward of good behavior in prison and the supervision of the paroles after release from prison is reformative. The prisoner who does not cause trouble and manifests industry expiates some of his offense against society and has given some assurance that he can live lawfully. It is also presumed, at least in part, that good conduct in prison is an evidence of true reformation and not of a desire to be released from prison.

Prisoners render meritorious services in prison, such as working in the barber shop, the kitchen, the

shoe shop, or the furniture shop, and this service is rewarded. The rendering of such service is encouraged by the warden and his administrators, and service as a subject in a medical experiment may be similarly encouraged and rewarded.

Since one of the purposes of the parole system is reformatory, the reformatory value of serving as a subject in a medical experiment should be considered. Serving as a subject in a medical experiment is obviously an act of good conduct, is frequently unpleasant and occasionally hazardous, and demonstrates a type of social consciousness of high order when performed primarily as a service to society. The extent to which the service of a prisoner in an experiment is motivated by good social consciousness on the one hand and by the desire for a reduction of sentence in prison on the other is a matter for consideration in the case of each prisoner.

Regardless of a prisoner's motives for volunteering for an experiment, an habitual criminal or a prisoner who has committed a notorious or heinous crime should not be considered an acceptable volunteer for a medical experiment.

As mentioned above, the most important requirement for the ethical use of human beings as subjects in medical experiments is that they be *volunteers*. Volunteering exists when a prison is able to say "yes" or "no" without fear of being punished or of being deprived of privileges due him in the ordinary course of events.

A reduction of sentence in prison, if excessive or drastic, can amount to undue influence. If the sole motive of the prisoner is to contribute to human welfare, any reduction in sentence would be a reward. If the sole motive of the prisoner is to obtain a reduction in sentence, an excessive reduction of sentence which would exercise undue influence in obtaining the consent of prisoners to serve as subjects would be inconsistent with the principle of voluntary participation (15).

MENTAL INCOMPETENTS AS SUBJECTS

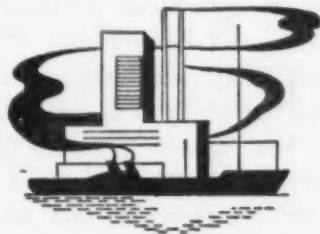
Mentally incompetent persons have on occasion been used as subjects in medical experiments designed to elucidate the cause and the treatment of mental

disorders. They have also occasionally been used as subjects in nutritional experiments and the study of the action of drugs which only indirectly might be related to the cause of mental disorders. In fact, the results of animal experimentation have perhaps less direct application to the study of the treatment of mental disorders in man than the results of animal experimentation in the treatment of other diseases. This means that in the treatment of mental disease, greater chances must be taken, as for example, when the convulsion, hyperthermia, and malaria treatments were first used for certain mental diseases. Even then, the hazards should be as carefully studied as possible in animals before the treatment to be tried is applied to the insane patient. As in amputating a limb, the extent of possible harm must be weighed against the extent of possible good for the patient treated.

The ethical principles involved in the use of the mentally incompetent are the same as for mentally competent persons. The only difference involves the matter of consent. Since mental cases are likened to children in an ethical and legal sense, the consent of the guardian is required.

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NEWS and Notes

G. H. Hart, head of the Division of Animal Husbandry of the University of California College of Agriculture, has been named chairman of the U. S. Committee for the 14th International Veterinary Congress, to be held in London August 9-14, 1949. Dr. Hart will organize the U. S. participation in the Congress and arrange transportation and accommodations for the 500 delegates expected to attend from the United States.

Philip M. Morse, director of the Brookhaven National Laboratory since September 1946, has resigned to return to his teaching and research activities in the Department of Physics of Massachusetts Institute of Technology. He will continue to serve the Laboratory as consultant. **Leland J. Haworth**, has been appointed acting director.

Haldon A. Leedy, acting director of the Armour Research Foundation of the Illinois Institute of Technology since March 12, has been named director.

Frank M. Semans, consulting biologist, has joined the staff of the Agriform Company, Inc. (agricultural chemicals), at Santa Ana, California.

Douglas McGregor, professor of psychology and executive director of the industrial relations section of Massachusetts Institute of Technology, has been appointed president of Antioch College, Yellow Springs, Ohio, effective September 1. Dr. McGregor succeeds **Algo D. Henderson**, who will become associate commissioner of education in charge of higher education for the State of New York.

Stewart S. Cairns, of Syracuse University, has been appointed head of the Department of Mathematics at the University of Illinois.

Jefferson Browder, at present consulting and attending neurosurgeon to several Brooklyn and Long Island Hospitals, has been named to succeed

Emil Goetsch, who is retiring as director of the Department of Surgery, Long Island College Hospital, after serving in this position for 29 years.

Joseph F. Volker has resigned as dean of the Tufts College Dental School to become dean of the new School of Dentistry at the University of Alabama.

Detlev W. Bronk, chairman of the National Research Council, has recently returned from a brief visit to Norway and Sweden, where he delivered three addresses, one on the occasion of the dedication of the newly established Nobel Institute of Neurophysiology in Stockholm.

C. W. Andrews, of St. John's, Newfoundland, has been appointed instructor in the Department of Biology at Washington Square College of Arts and Science, New York University.

Grants and Awards

In what is in many ways a unique program for encouraging students with special aptitudes to engage in scientific careers, the University of Rochester on June 11 announced the 5th annual award of 5 Bausch & Lomb Science Scholarships, valued at \$1,500 each.

The successful candidates, shown on this week's cover, are, beginning at top left, William C. Luft, Goshen, New York; Raymond A. Santirocco, Rochester, New York; Edwin D. Becker, Jr., Columbia, Pennsylvania; Nancy Lee Greenwood, Falls Church, Virginia; and Richard F. Bakemeier, Indianapolis, Indiana.

The winners were chosen in a nationwide competition. From an original group of more than 1,100 high school seniors who made application or inquiry, 443 were selected as qualified candidates. From these, 20 finalists from 12 states were invited to go to the University of Rochester on May 21-22 for final aptitude and other tests, and interviews.

As has been the case each year since the program was initiated in 1944 by the Bausch & Lomb Optical Company and the University of Rochester, the competition was so close that the University awarded 7 other

scholarships of approximately equal value to other finalists in addition to the 5 Bausch & Lomb awards. All 12 have accepted and will attend the University of Rochester as freshmen in September.

The new group will bring to a total of 45 the number of outstanding students who have attended the University in the last 5 years as a direct result of the Science Scholarship Program. Of the 45, 23, including 5 girls, have won Bausch & Lomb Scholarships, and 22 were finalists to whom the University awarded others of its major scholarships. These students came from 24 states from Maine to California, and from both cities and small towns. They are a select group, with outstanding intellectual capacities and attainments, who share special aptitudes in scientific and allied subjects and show promise of becoming leaders in their chosen fields.

Personality factors and breadth of interests are taken into account by the University's Scholarship Committee which makes the selections, in the belief that today's scientists not only must be experts in their fields, but also must be alert to broad social and political trends and to the responsibility which science owes to society.

In every instance, students holding the scholarships have combined superior academic performances with campus leadership. In addition, they have shown maturity of purpose and enthusiasm and broad interests which range from music and art to athletics, politics, dramatics, and religion. There is significance, too, in the fact that a majority of them take an active part in college religious activities. Nearly all are members of one or another of the organizations which foster this phase of student life.

The Science Scholarship Program grew out of the Bausch & Lomb Honorary Science Award Plan introduced in 1932 and now conducted in more than 4,800 secondary schools of the country, under which a medal is given annually in each participating school to the graduating student who has maintained the highest standing in scientific subjects. As an extension of this plan, the company introduced the scholarship awards in 1944. Only

those students who have won the Honorary Science Award medal are eligible to compete for the scholarships.

The sole purpose of the program is to encourage scientific training for students who have proved their ability to make good use of it. M. Herbert Eisenhart, president of the company and also chairman of the University of Rochester Board of Trustees, and his associates are convinced that this Nation's future development will depend in large measure upon its scientific advances and that it faces a serious shortage of scientists. Bausch & Lomb as an optical industry is highly dependent upon science and for that reason is keenly aware of the need for providing education and opportunity for the priceless national asset of young men and women of promising talent.

Educators have long emphasized, and the war made it even more urgent, that there must be many more trained young persons in scientific fields. In the combined medal award and Science Scholarship Program, Bausch & Lomb has found a practical tie-up between the schools and industry, the academic and the practical, which will assist in assuring an increased flow of trained minds into vital industries, fields of research, and teaching.

Lalor Foundation Fellowships at the Woods Hole Marine Biological Laboratory for the current summer have been awarded to nine investigators. Four former fellows have been reappointed: Irving Klotz, Northwestern University; Arnold Lazarow, Western Reserve University; Benjamin Libet, University of Chicago; and Claude Villee, Harvard University. New appointments include: Avram Goldstein, Harvard University; Joseph Lein, Syracuse University; Harold Persky, Michael Reese Hospital, Chicago; and Warren H. Yudkin, Yale University. In addition, a special fellowship has been awarded to Ernest Baldwin, of the University of Cambridge, England, comparable to that awarded last year to Jean Brachet, from the University of Brussels.

The Lalor Foundation Fellowships are awarded in the fields of biochemistry, biophysics, and biological chem-

istry and are designed primarily to aid young investigators by providing laboratory facilities and the opportunity to associate at Woods Hole with distinguished investigators in these fields.

A Frederick Gardner Cottrell Grant of \$8,500 for use in special research in physics has been made to Carleton College by the Research Corporation, New York City, according to an announcement by Dr. Laurence M. Gould, president of the college.

The grant is made to the Department of Physics for the term of one year for research on the application of nuclear resonance absorption techniques to study of gases and gas-liquid phase changes. Funds are immediately available for the procurement of equipment and for providing fellowships for technical assistants.

Research under the new grant will be directed by Frank Verbrugge, chairman, and Robert L. Henry, assistant professor in the Department of Physics.

Meetings

A Conference on the Biological Applications of Nuclear Physics scheduled for July 26-30 has been announced by the Biology Department of the Brookhaven National Laboratory. The 5-day program has been planned as follows: Monday, July 26, session on health physics with B. S. Wolf, Atomic Energy Commission, New York, C. R. E. Merkle, of Brookhaven, G. Failla, of Columbia, and F. P. Cowan, of Brookhaven, participating; Tuesday, July 27, applications of radiocarbon, radioiron, and radiophosphorus compounds, with W. M. Miller, L. M. Sharpe, and J. Sacks, of Brookhaven, participating, together with N. R. Radin, of Columbia University, and A. S. Keston, of New York University. The final 3-day period will be devoted to a symposium on radioiodine. The Wednesday session will consider physiology. W. T. Salter, of the Yale School of Medicine, will be chairman of this meeting, at which R. Rawson, of the Memorial Hospital, New York City, B. Skansa, of Massachusetts General Hospital, Boston, and E. B. Astwood and M. M. Stanley, of the Pratt Diagnostic Hospital, Bos-

ton, will present papers. The Thursday morning session, on laboratory topics, will be led by L. F. Nims, of Brookhaven, and will include papers by S. Feitelberg, of Mt. Sinai Hospital, Edith Quimby, of the College of Physicians and Surgeons, Eleanor Oshry, of Montefiore Hospital, and Charlotte Schmidt, Presbyterian Hospital, all of New York. At the Thursday afternoon session, under the chairmanship of S. Hertz, of the Beth Israel Hospital, Boston, hyperthyroidism will be discussed by E. M. Chapman, of Massachusetts General Hospital, M. Soley, of the State University of Iowa, and S. C. Werner, of the Presbyterian Hospital, New York. The Friday morning session, on pathology and allied topics, with L. Craver, of Memorial Hospital, New York, presiding, will include papers by P. J. Fitzgerald, and L. D. Marinelli and Ruth Hill, of the Memorial Hospital, and T. C. Evans, of the University of Iowa. At the final afternoon session on July 30, cancer will be discussed by S. M. Seidlin, of the Montefiore Hospital, and J. B. Trunnell, of the Memorial Hospital, New York; B. Parsons of the Presbyterian Hospital, New York will be chairman of this meeting.

Applications for registration and inquiries regarding the conference should be addressed to Ellen Matteson, Brookhaven National Laboratory, Upton, New York. Reservations for attendance at the conference will be filled in order of their receipt.

The Fifth Annual Seminar for the Study and Practice of Dental Medicine will be held at the Desert Inn, Palm Springs, California, October 17-21, Dr. Hermann Becks, Seminar president, has announced. One of the foremost topics to be discussed will be the topical application of fluoride. This subject will be reviewed in great detail, and various methods recommended for its administration for the prevention and control of dental caries will be evaluated. In addition, 9 leading authorities in the fields of dental caries, inflammation, paradentosis, clinical oral pathology, and experimental biology will submit papers and lectures during the session this year. Further information may be secured by writing to Marion G. Lewis,

Executive Secretary, 1618 Ninth Avenue, San Francisco 22, California.

UNESCO Sponsors Two Conferences on Scientific Abstracting

The first meeting of the Interim Coordinating Committee on Medical and Biological Abstracting took place on April 5-6. The establishment of this Committee under the Division of Natural Sciences of UNESCO was recommended by a Conference on Abstracting held in Paris last October, and the same chairman and vice-chairman—Dr. Hugh Clegg, of the British Medical Association, and Mrs. Eileen R. Cunningham, of Vanderbilt University Medical School and the Medical Library Association—were reappointed. Other members present were: Dr. F. Donker Duyvis, secretary-general of the International Federation for Documentation; Dr. G. M. Findlay, editor of *Abstracts of World Medicine*; Dr. Leslie Lampitt and Prof. Samson Wright, of *British Abstracts*; Prof. M. W. Woerdeman, editor of *Excerpta Medica*, Amsterdam; and Dr. A. Hahn, of the International Federation of Library Associations. Dr. John E. Flynn, editor of *Biological Abstracts*, also on the Committee, was unable to attend because of illness.

Observers present included Mr. Louis Gros, of the United Nations; Dr. E. J. Crane, editor of *Chemical Abstracts*; Dr. Howard-Jones and Mr. Z. Deutschman, of the World Health Organization; and Prof. E. Velandar of the Ingeniors Svetanskaps Akademien, Stockholm.

Members of the UNESCO Secretariat present were: Dr. J. Needham, Prof. Pierre Auger, Dr. I. M. Zhukova, and Mr. J. B. Reid; Mr. E. J. Carter and Mr. A. Møller, of the Libraries Section; Dr. Thompson, UNESCO representative in Germany; and Mr. F. Hepp, of the Copyright Section.

After greetings from Dr. Walter Laves, deputy director-general, and from Dr. Needham, chief of the Natural Sciences Section, a summary report was made by Dr. Zhukova. Among the constructive gains reported since the Conference held last October were:

(1) Authorization by the General Conference of UNESCO to set up the

Coordinating Committee on Medical and Biological Abstracting under the Natural Sciences Section and to ask the cooperation of the World Health Organization in the project.

(2) Initiation and increase of cooperation between various British abstracting services by means of the exchange of abstracts and information, and between these services and *Biological Abstracts* and *Chemical Abstracts*.

Excerpta Medica has now completed the legal formalities necessary to enable it to operate under Dutch law governing nonprofit organizations and expects Government approval shortly; it will operate under a Board of Trustees consisting of professors of Dutch universities. A special discount price of \$250 for this publication has been granted libraries in the United States who subscribe to all sections; the usual price is \$342.50. One of the factors which made this arrangement possible was the cooperative attitude of Williams and Wilkins, the American agents for this journal. Ways and means are being studied so that a similar discount can be offered to libraries of other countries. This has been more difficult to arrange, due to the attitude of the European book agents and their methods of distribution; however, it is believed that some solution to the problem will soon be found.

From the standpoint of elimination of duplication and overlapping of services, the results have so far been disappointing. It is obvious that gains here will be slow and that much educative work will be necessary before any real pooling of resources or coordination of services can be expected. It was recognized that the Coordinating Committee, while necessarily concerning itself at present chiefly with practical details, should not lose sight of its educative functions and should keep constantly on the agenda this ultimately desirable goal.

The permission given by occupation authorities enabling the Springer Publishing Company to resume the publication of the German abstracting journals at prewar prices further complicates the picture. Authority to do so was granted through IPEX, which is a joint agency. UNESCO has been asked to inform the authori-

ties of the conclusions reached by this Committee and of its interest in the matter.

The need for *Biological Abstracts*, *British Abstracts*, and *Excerpta Medica* to come to some agreement in regard to the coverage of nonclinical subjects was stressed.

It is obvious that the slowness of publication which besets the larger comprehensive services accounts in part for the multiplicity of highly specialized abstracting services. The reluctance of the editors of such services to utilize authors' abstracts of articles published in reliable scientific journals, though this would facilitate almost simultaneous publication of both article and abstract, is another reason why it will be some time before much gain can be hoped for.

Certain recommendations were made: (1) that the World Health Organization and the Food and Agriculture Organization be invited to join UNESCO in sponsoring the activities of the Committee on Medical and Biological Abstracting; (2) that a representative for the medical and biological abstracting services in France be appointed; (3) that the American Medical Association be invited to become a member; (4) that certain other abstracting services operating on a similar basis to those already admitted be invited to become members.

An Executive Committee was set up in order to facilitate the carrying on of business by correspondence.

The need for language editions of Abstracting Services is still being investigated. The World Health Organization was asked to invite the cooperation of BioMedgiz in regard to Russian literature, and UNESCO's Latin-American Field Science Co-operation Office is investigating the needs of the Spanish- and Portuguese-speaking countries.

It was decided to find, if possible, a reputable publisher willing to undertake preparation of extensive polyglot glossaries of the Medical and Biological Sciences.

Certain practical proposals for cooperation between services were discussed. (A more detailed report will be published in the Bulletin of the Medical Library Association.)

The Expert Committee on Scien-

tific Abstracting met April 7-9 under the auspices of the Natural Sciences Section. Dr. Alexander King, of the Lord President's office in London, served as chairman and Prof. E. Velander, of the Ingeniors Svetanskaps Akademien, Stockholm, as vice-chairman. Other participants were Prof. J. D. Bernal; Sir David Chadwick, former Secretary of the Imperial Agricultural Bureaux, London; Dr. E. J. Crane; Prof. F. Cuta, Technical University, Prague; Mrs. Eileen Cunningham; Dr. Donker Duyvis; and Prof. Wyart, of the Centre du Documentation du Centre National de la Recherche Scientifique, Paris. Members of the UNESCO Secretariat attending were Dr. Joseph Needham, Prof. Pierre Auger, Mr. J. B. Reid, Dr. I. M. Zhukova, Mr. E. J. Carter, Dr. A. Møller, and Dr. Mollina.

UNESCO's interest in the problem is very direct. By its constitution it is instructed to "maintain, increase, and diffuse knowledge . . . by initiating methods of international co-operation calculated to give the peoples of all countries access to the printed and published materials produced by any of them."

The main purpose of the Conference was to plan for a larger International Conference on Science Abstracting to be held later in the year under the auspices of UNESCO. There was unanimous agreement that to hold such a conference was not only desirable but absolutely necessary. The details of arrangement and the date were to be decided by the UNESCO Secretariat, who would have the responsibility for handling it.

All were agreed that the agenda should emphasize possible methods of practical achievement. Opportunity should be given for different countries to clarify their ideas to realize the enormity of the problem and the need for simplification.

Dr. Alexander King mentioned the fact that the British Commonwealth Scientific Information Conference, to be held in London the end of June and to be limited to the Commonwealth and a few delegates from the U.S.A., would in no way take the place of the proposed International Conference on Abstracting. He felt that from the discussions of abstracting and indexing some valuable working data might

be made available to the International Conference.

It was pointed out that librarians and documentalists have hitherto been those chiefly concerned over the abstracting situation, while the scientists themselves have, to a great extent, ignored it. Many present expressed the opinion that conditions have now become so chaotic that scientists will be compelled to aid in seeking some solution.

It was also brought out again and again during the Conference that the problem was primarily that of rendering efficient service for science and that it could not be solved by any one group alone. The advantage of a representation which afforded a combination of the ideas and views of scientists, editors of abstracting services, librarians, and those concerned with documentation (as was the case during the present Conference) was obvious, and it was recommended that this combination be carried forward into the framework of the larger proposed international conference.

It was also obvious that UNESCO, with its facilities for holding conferences, its excellent interpreters and stenographic aid, and its facilities for the production and planning of agenda, working papers, charts, and documents, represents for the present the ideal agency under which to nurture solutions to the problems pertaining to abstracting in the sciences. Later it may be possible to organize a World Council of Scientific Abstracting, possibly closely associated with the International Council of Scientific Unions.

UNESCO's excellent policy of calling in various international organizations to aid in certain specific phases of the work assures that expression will be given to many types of opinions and that the work will receive different types of aid. An example of this was evidenced by the very helpful contribution made by the International Federation of Documentation in its preliminary list of existing abstracting services and a report which it submitted. It was recommended that a revised and evaluated form of this list be used as a working paper for the future conference.

High praise is due the UNESCO Secretariat, who lay every facility of

an excellent organization at the disposal of delegates to conferences, are ever ready to answer questions, are prompt to give aid on request, and yet miraculously manage to turn the conference, itself, over to the delegates and even refrain from expressing decided opinions.

Thanks to the alert library service of UNESCO, examples of many different types of abstracting journals were available. Bibliographies of articles on abstracting and a film illustrating the use of the Bush electronic selector for references, which is still in an experimental status at the Department of Agriculture Library in Washington, were made available to delegates. (EILEEN R. CUNNINGHAM, *Chairman, Committee on a Coordinated Abstracting Service for Clinical Medicine, Medical Library Association.*)

Deaths

Oscar Edward Meinzer, 71, president of the American Geophysical Union and internationally known geologist, died June 14 at his home in Washington, D. C. From 1912 until his retirement in 1947, Dr. Meinzer had also served as chief of the ground water division, U. S. Geological Survey.

William Edgar Lower, 81, a founder of the Cleveland Clinic Hospital and former associate professor of surgery at Western Reserve University, died June 17 in Cleveland, Ohio.

George A. Soper, 78, sanitary engineer and epidemiologist, died June 17 at the Southampton Hospital, Southampton, L. I., New York. Dr. Soper was the discoverer of the typhoid carrier, "Typhoid Mary."

Frederic B. Knight, 56, head of the Purdue University Division of Education and Applied Psychology since 1937, died June 19 at Lafayette, Indiana.

Harry Diamond, 48, chief of the electronics division of the National Bureau of Standards, died suddenly June 21 in Washington, D. C., as the result of a heart attack. Dr. Diamond was one of the group responsible for the development of the radio proximity fuse.

Comments and Communications

Angular Correlation of Scattered Annihilation Radiation

Under the above title, Snyder, Pasternack, and Hornbostel (quoted in this note as SPH; *Phys. Rev.*, 1948, 73, 440) published a calculation of the cross section for coincidence measurements of the scattering of two photons, emitted in the annihilation of a positron and a negatron. The same result was independently derived by Pryce and Ward (*Nature, Lond.*, 1947, 160, 435), who did not give their method for obtaining this result. It has recently been checked experimentally by Bleuler and Bradt (*Phys. Rev.*, 1948, 73, June 1).

SPH derive the expression for the cross section in two different ways. One is by the usual perturbation theory methods; the second, by what they call the partial polarization analysis method. We wish to give here an admittedly crude and far from rigorous derivation of the final formula which seems to us to show more clearly what is done and which physical assumptions were implied in the partial polarization method. Although there is no essential difference between this method and that given in the paper of SPH, we believe that the method given here is easier to understand.

As has been emphasized often, the two photons produced at the annihilation of the positron and the negatron (in a singlet state) will be polarized in such a manner that if one of them shows a right-hand circular polarization, the other will show a left-hand circular polarization,¹ since the total angular momentum after the annihilation has to be zero as it was before the annihilation. This situation is equivalent to the situation where the two photons are linearly polarized perpendicular to each other. In order to show this often-quoted result, we may consider the wave function describing the two photons, given by

$$\varphi = \frac{1}{\sqrt{2}} [\varphi_1(l)\varphi_2(r) - \varphi_1(r)\varphi_2(l)],^2$$

where $\varphi_i(l)$ is the wave function of the i -th photon, with

¹This definition of right-hand and left-hand circular polarization is different from the usual one. We have followed the description of SPH, and others. If one, however, uses right- and left-hand polarization in the way it is defined in most textbooks, i.e. referred to the direction of propagation of the photon and not to a fixed system of reference, as is done here, one should say that the two photons are either both right- or both left-hand polarized.

²The negative sign is necessary because φ describes the polarization for the case where the circular polarizations are of opposite sign. There ought to be included an also antisymmetric part describing the movement of the two photons in opposite directions. The fact that φ is antisymmetric is analogous to the fact that for a singlet state of a two-electron system, the spin function is antisymmetric (see, for instance: H. A. Kramers, *Hand- und Jahrbuch der Chemischen Physik*. (Bd. I.) Leipzig: Akademische Verlagsgesellschaft, 1938; and G. Wentzel, *Quantentheorie der Wellenfelder*. Vienna: Deuticke, 1942).

a left-hand circular polarization. If we now change from circular polarization to linear polarization, we have to use the transformation (cf. W. Pauli, *Handbuch der Physik*. (Vol. 24, Pt. 1), Berlin: Springer, 1933).

$$\varphi(l) = \psi(\alpha) \cos \omega t + \psi\left(\alpha + \frac{\pi}{2}\right) \sin \omega t,$$

$$\varphi(r) = -\psi(\alpha) \sin \omega t + \psi\left(\alpha + \frac{\pi}{2}\right) \cos \omega t,$$

where $\psi_i(\alpha)$ is the wave function of the i -th photon which is polarized in a direction making an angle, α , with a fixed plane. In this way, we get

$$\psi(\alpha) = \psi_1(\alpha) \psi_2\left(\alpha + \frac{\pi}{2}\right) - \psi_1\left(\alpha + \frac{\pi}{2}\right) \psi_2(\alpha).$$

Since the direction of the polarization of one of the photons is arbitrary, we can write for the wave function of the system:

$$\psi = \frac{1}{2\pi\sqrt{2}} \int_0^{2\pi} d\alpha [\psi_1(\alpha) \psi_2\left(\alpha + \frac{\pi}{2}\right) - \psi_1\left(\alpha + \frac{\pi}{2}\right) \psi_2(\alpha)].$$

We see here that ψ describes a situation where both photons are unpolarized, but are polarized perpendicularly to each other (compare SPH). We wish now to discuss first the case of the (nonrelativistic) photo effect, i.e. the case where the photons eject electrons in the direction of their polarization. We are especially interested in the probability that the two photoelectrons are ejected in directions which make an angle, ϕ , with each other. That is, we have to look for the amplitude of the function $\psi_1(0) \psi_2(\phi)$ in ψ , if we take the fixed plane, mentioned above, through one of the counters which are counting the photoelectrons. In order to determine that amplitude, we write

$$\psi_1(\beta) = \cos \beta \psi_1(0) + \sin \beta \psi_1\left(\frac{\pi}{2}\right),$$

$$\psi_2(\beta) = \cos(\beta - \phi) \psi_2(\phi) + \sin(\beta - \phi) \psi_2\left(\phi + \frac{\pi}{2}\right),$$

and we get

$$\begin{aligned} \psi = \frac{1}{2\pi\sqrt{2}} [& (-\int \cos \alpha \sin(\alpha - \phi) d\alpha) \psi_1(0) \psi_2(\phi) + \\ & (\int \cos \alpha \cos(\alpha - \phi) d\alpha) \psi_1(0) \psi_2\left(\phi + \frac{\pi}{2}\right) + \\ & (-\int \sin \alpha \sin(\alpha - \phi) d\alpha) \psi_1\left(\frac{\pi}{2}\right) \psi_2(\phi) + \\ & (\int \sin \alpha \cos(\alpha - \phi) d\alpha) \psi_1\left(\frac{\pi}{2}\right) \psi_2\left(\phi + \frac{\pi}{2}\right) - \{2, 1\}] \end{aligned}$$

or

$$\psi = \frac{1}{\sqrt{2}} \left[\sin \phi \psi_1(0) \psi_2(\phi) + \cos \phi \psi_1(0) \psi_2\left(\phi + \frac{\pi}{2}\right) - \cos \phi \psi_1\left(\frac{\pi}{2}\right) \psi_2(\phi) + \sin \phi \psi_1\left(\frac{\pi}{2}\right) \psi_2\left(\phi + \frac{\pi}{2}\right) \right]. \quad (1)$$

Since the four functions, $\psi_1(0) \psi_2(\phi)$, $\psi_1(0) \psi_2\left(\phi + \frac{\pi}{2}\right)$, $\psi_1\left(\frac{\pi}{2}\right) \psi_2(\phi)$, $\psi_1\left(\frac{\pi}{2}\right) \psi_2\left(\phi + \frac{\pi}{2}\right)$, are orthogonal wave functions, we immediately obtain from equation (1) the probability for the above-mentioned situation. That probability is $\frac{1}{2} \sin^2 \phi$, already mentioned by Pryce and Ward.

We may express equation (1) in the following way. The situation from which we start is fourfold degenerate, and four orthonormal wave functions pertaining to this

state are $\psi_1(0)\psi_2(\phi)$, etc. Since only one of the four functions contributes to the phenomenon we want to observe, we obtain the probability for that phenomenon immediately from the square of the amplitude.

The process mentioned in the beginning of this note is, however, not so simple, since, also, photons polarized perpendicularly to the plane of scattering contribute to the coincidences. If and only if the four functions used in the expansion in equation (1) represent an orthonormal set for the fourfold degenerate state, we can use equation (1) to calculate the cross section for the above-mentioned process. For this cross section, we can write:

$$\sigma = \sum a_k^2 \sigma_k, \quad (2)$$

where the a_k represent the amplitudes of the functions $\psi_1(0)\psi_2(\phi)$, etc., and σ_k are the cross sections for the photons in the directions considered. For the function $\psi_1(\alpha)\psi_2(\beta)$, the cross section is, apart from a normalizing factor,

$$\sigma_k = (\gamma_1 - 2 \sin^2 \theta_1 \cos^2 \alpha) (\gamma_2 - 2 \sin^2 \theta_2 \cos^2 \beta), \quad (3)$$

where the θ_i and γ_i have the same meaning as in the paper by SPH. From equations (1) to (3) we finally get, again apart from a normalizing factor

$$\sigma = \gamma_1 \gamma_2 - \gamma_1 \sin^2 \theta_2 - \gamma_2 \sin^2 \theta_1 + 2 \sin^2 \theta_1 \sin^2 \theta_2 \sin^2 \phi, \quad (4)$$

which is identical with the result of SPH or Pryce and Ward.

If the four functions used in equation (1) had not been an orthonormal set, equation (2) should have included cross terms with $a_k a_m$, and we ought first to orthonormalize the set of functions used before applying an equation such as equation (2).

The fact that our choice, which is the natural, obvious choice makes it possible to use equation (2), corresponds to the remark of SPH that one has to resolve the polarizations of the photons in this particular way. It also corresponds to the fact that, only for this particular choice of the system of reference, the cross terms in SPH's equation (13) obtained by the usual perturbation theory vanish, as was also remarked by SPH.

The final cross section (4) may also be obtained by treating the scattering as consisting of two parts, an isotropic and an anisotropic part. One can then again use a formula, analogous to equation (2). If one chooses the right frame of reference, the result is the same.

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Formation of Itacolumite

Itacolumite, a stratified flexible sandstone, consists of symmetrically arranged rows of interlocking quartz crystals. In the study of its mode of formation, previous workers limited themselves in the main to general observations on field characteristics without considering the conditions essential to its formation. Again, extensive work has been carried out on the effect of fluxes upon the transition temperatures of quartz, though without reference to the problem under review.

A survey of the field observations shows that specimens taken from different localities vary both in their mineral

associations and their degree of metamorphism. The rock matrix may, for example, comprise mica flakes along the bedding planes and as a joint between the quartz crystals (Itacolumi, Minas Geraes, Brazil—Schulz. *Bull. Soc. Geol. France*, 1834, 416; Gergens. *Neues Jahrb.*, 1841, 566; Zerrener and Von Humbolt. *Z. dtsh. geol. Ges.*, 1849, 484); it may consist of traces of muscovite and unevenly distributed clay (Delhi—Mügge. *Neues Jahrb.*, 1887, 1, 195), sometimes soft felspathic materials form the matrix (Kaliāna, India—Falconer. *J. Soc. Bengal*, 1847, 6, 240; Medlicott. *Rec. geol. Surv. India*, 1874, 7, 30), and, again, calcium carbonate may be the cementing agent (Chārli, Berar—Hughes, who quotes Fedden. *Mem. geol. Surv. India*, 1877, 16). These, together with Derby's observations (*Amer. J. Sci.*, 1884, 28, 205) of weathered itacolumite as a purely quartz entity, illustrate the wide variety in composition.

The range in degree of metamorphism is equally marked, for the Brazilian and Kaliāna specimens have their mica flakes arranged with their longer axes parallel, suggesting considerable pressure and squeezing. Buschendorf (*Fort. Min. Krist. Pet.*, 1933, 17, 407) has described the compression of individual quartz grains in the Kaliāna material—again signifying intense metamorphism, while the flexible sandstone discovered by Fedden, though exhibiting all the characteristics of itacolumite, contains calcium carbonate and shows virtually no metamorphism.

A study of the influence of fluxes upon the transition of amorphous silica to quartz goes to show that, though the mineral associations are diverse in type, they are of definite importance in the formation of itacolumite.

For quartz crystals to be formed, molecular mobility is essential and is, no doubt, attained either by fusion or by solvent action. With regard to fusion, the high temperatures involved may lead to nondifferentiation between the lower and higher forms of quartz, the additional formation of tridymite and cristobalite, and possibly the twisting and twinning of the quartz crystals. It has been shown, furthermore, that by this pyrogenic method, there is a tendency for silica to separate as a metastable, solid, vitreous mass when concentrations are high, cooling is rapid, and nuclei are absent. In contrast, the hydrothermal process, involving a variety of fluxes, actually facilitates the transition to quartz at much lower temperatures. It thus eliminates most of the anomalies cited.

Confining our attention to the latter, a number of experimenters have demonstrated this facility in the case of particular fluxes. The transition of amorphous silica to quartz occurs in the region of 870°. The temperature is depressed and the time factor lowered in the presence of water and solutions of lithium chloride-oxychloride. It is reduced to 750° with sodium or lithium tungstate, to 350°–380° with hydrofluoboric acid, and to 300° in the presence of sodium metasilicate and sodium chloride. Again, quartz has been obtained by heating silicic acid gel with potassium or sodium carbonate at 350°–390° and by the action of sodium carbonate and bicarbonate on aluminosilicate gels at 255°–355°.

The rhythmic deposition of quartz crystals would be brought about in a system specific to the Liesegang phe-

nomenon—a system in which the constituents, acting as fluxes, influence the course of diffusion interaction, and transition. The itacolumite matrix is therefore indicative of the physical conditions prevailing during the formation of the mineral. Deviations from these conditions may be readily seen, as in the South Carolina deposits, where beds of itacolumite pass into stratified and even massive quartzite (Tuomey. *Report on the geology of South Carolina*. Columbia, 1848. Pp. 9, 78). The assumption that certain matrices are due to secondary depositions is doubtful in view of the fact that the metamorphism of the mineral associations closely follows that of the itacolumite itself.

Thus, while silicic acid gels give rise to minerals of the hydrated silica type (flint, opal, agate, etc.) and may be viewed as a transition of a secondary to a tertiary polymer of silicic acid, and while a silica-rich magma may lead eventually to the separation of massive quartzite, the formation of itacolumite is probably brought about by the action of various acidic substances on the basic fluxes, the fluxes serving as solvents of silica or in combination with it, the reaction taking place under conditions inherent to periodicity.

In the course of recent work (A. C. and M. Copisarow. *Nature, Lond.*, 1942, 149, 413; 1946, 157, 768; *J. Amer. chem. Soc.*, 1945, 67, 1915; *Science*, 1946, 104, 286), periodic formations of amorphous silica and silicic acid gel were obtained by the interaction of waterglass with acids. These rhythmic structures show a close analogy with itacolumite. Extending these experiments, therefore, to temperatures above the transition of amorphous silica to quartz, the conditions essential to the formation of itacolumite should be attained. In this case, the interband or embedding material would consist of the reaction product between the flux and the acidic or saline reagent.

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Effect of the Protein Content of the Diet on the Glomerular Filtration Rate of Young and Adult Rats

Inulin clearances in rats have been estimated by several authors. Their results, however, do not seem to agree with reference to (a) the relation between the rate of glomerular filtration and that of urine flow and (b) the mean value of the glomerular filtration rate. Some workers (S. E. Dicker and H. Heller. *J. Physiol.*, 1945, 103, 449; 104, 31; S. M. Friedman, J. R. Poley, and C. Friedman. *Amer. J. Physiol.*, 1947, 150, 340; R. W. Lippman. *Amer. J. Physiol.*, 1947, 151, 211) found that the glomerular filtration was independent of the urine flow, resembling in this respect adult man and the dog; others (E. Braun Menendez and H. Chiodi. *Rev. Soc. Arg. Biol.*, 1946, 22, 314; M. Friedman. *Amer. J. Physiol.*, 1947, 148, 387) claimed that the rate of glomerular filtration varied directly with the urine flow, as in rabbits.

Work on other species as well as on rats suggests at

least two factors which may have operated in producing these confusing results. The rate of glomerular filtration is independent of that of urine flow in adult human beings, but correlated with the urine flow in infants (H. L. Barnett. *Proc. Soc. exp. Biol. Med.*, 1940, 44, 654; R. F. A. Dean and R. A. McCance. *J. Physiol.*, 1947, 106, 431). Also, there is a strong indication that nutritional factors influence the rate of glomerular filtration in animals (J. A. Shannon. *Amer. Rev. Physiol.*, 1942, 4, 309; S. E. Dicker and H. Heller. *J. Physiol.*, 1945, 103, 449; 104, 31; S. E. Dicker. *Brit. J. Pharmacol.*, 1946, 1, 194; S. E. Dicker, H. Heller, and T. F. Hewer. *Brit. J. exp. Path.*, 1946, 27, 158).

The influence of age and diet on the glomerular filtration rate of rats was therefore investigated. Inulin clearances were estimated (a) in adolescent rats with body weights ranging from 101 to 150 gm and (b) in adult rats (weights, 275–320 gm) fed on a diet containing varying amounts (7, 14, 18, and 25%) of casein.

TABLE 1

	Plasma proteins (gm/100 ml)	Glomerular filtration rate (ml/100 gm/min)	r	b
Young rats (101.0–150 gm)	5.23	Correlated with urine flow	+0.778 ±0.073	+10.02
Adult rats (265.0–325.0 gm) 7% casein	5.84		+0.462 ±0.172	+ 6.39
Adult rats (270.0–345.0 gm) 14% casein	6.44		+0.415 ±0.166	+ 3.32
Adult rats (265.0–350.0 gm) 18% casein	6.83	0.43 ±0.009	–0.243 ±0.200	– 1.21
Adult rats (260.0–330.0 gm) 24% casein	7.33	0.76 ±0.035	–0.206 ±0.220	– 0.90

r = correlation coefficient between glomerular filtration rate and urine flow, b = regression coefficient. Values are means and standard error.

The results of the inulin clearance estimations in these series (Table 1) show clearly that, in adolescent rats as well as in adult rats fed on a diet low in casein, the rate of glomerular filtration was correlated with that of the urine flow, but that, in adult rats fed on a diet containing at least 18% casein, the rate of glomerular filtration was independent of the urine flow. It can also be seen that raising the amount of casein in the food, and thus the plasma protein level, produced an increase in the rate of glomerular filtration (Table 1).

It can thus be concluded that the disagreement between the authors interested in the kidney functions of the rat is only apparent. If the animal material is standardized, viz., due consideration is paid to the age and diet of the rats used, uniform results can be expected.

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Cytogenetic Effects in Corn Exposed to Atomic Bomb Ionizing Radiation at Bikini

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The biological experiments conducted at Bikini by the Naval Medical Research Section, Operation Crossroads, included tests of the effects of the ionizing radiation on both plants and animals.¹ Plants could be used advantageously in the genetic experiments, since large numbers of individuals are obtainable from small quantities of seeds which could be transported readily to and from the target area, and the plants could be grown wherever desired for observation and cytogenetic analysis. Dry seeds tolerate heavy doses of radiations such as gamma rays and X-rays without loss of viability and may be used to determine the biological effects of high intensities of ionizing radiation.

It must be realized that the genetic changes to be reported here are not directly applicable to man, since the amount of radiation received by the seeds would be lethal to man or animals. Corn was selected for these studies because of its tolerance for heavy doses of ionizing radiation and its suitability for both cytological and genetic studies of radiation effects, and because of the wealth of available information concerning its chromosome mechanism of heredity.

The effective radiations of the atomic bomb were compared with known doses of X-rays with respect to their action in causing direct injury to the seed and the plants grown from the seeds, and in producing visible chromosomal alterations. The heritability of the induced alterations causing pollen sterility also was studied. The samples of corn, chosen because of their uniform genetic constitution and suitability for cytological analysis of their pachytene chromosomes, included a commercial dent first-generation hybrid of two inbred lines (L289 × I205) and an inbred line of sweet corn (P51).

The corn seed was thoroughly air dried, placed in 25 moisture-proof packets, each containing from 1,500 to 2,500 seeds of the two kinds, and enclosed in canvas rolls

¹ Capt. R. H. Draeger, Officer in Charge of the Naval Medical Research Station, M. T. Jenkins, and L. J. Stadler assisted in planning the experiments reported here, and the assistance of E. G. Anderson and K. L. Retherford in growing the plants and collecting the data on plant sectors is gratefully acknowledged. Cooperating agencies included the Division of Cereal Crops and Diseases, Agricultural Research Administration, U. S. Department of Agriculture; the Department of Botany, Cornell University; and the Division of Biology, California Institute of Technology.

before being placed aboard the *S. S. Burleson* in charge of Joint Task Force One of the Navy for transfer to Bikini. The seed packets were distributed on 22 ships in the target area ranging in distances up to 1,500 yards from the target ship. The placement of the seed protected them from thermal radiation, air blast, and contamination by fission products other than ionizing radiations generated by the explosion of the bomb. Control samples were retained aboard the *Burleson* outside the target area and at Beltsville, Maryland. The explosion of the atomic bomb to which the seeds were subjected took place on July 1, 1946.² Following the explosion the Bikini samples were returned to Washington by air express.

The design of the experiments included a comparison of the effects of the radiations from the bomb with measured doses of X-ray. Additional samples of the same kinds of corn that were used in the Bikini test were irradiated within a few days of the time the bomb was exploded with unfiltered X-rays from a tungsten target tube operated at 80 KVP. Doses of 5,000, 10,000, 15,000, 20,000, and 25,000 r were applied to the seeds at the rate of 1,000 r/min, approximately 2,000 seeds being included in each sample.

Test plantings of the bombed and X-rayed seed were made at Beltsville as soon as the samples arrived from Bikini. The plants were inspected in the seedling stage on July 29. Field plantings of selected samples which included untreated controls were made immediately thereafter at the Experimental Farm of the California Institute of Technology in Arcadia, California.

The germinability of the seed was not affected by the radiations from the bomb or by the X-ray treatments utilized in these experiments. The growth of the plants from the bombed sample nearest the target (sample A) and from X-rayed samples treated with 10,000 and 15,000 r was noticeably retarded in the seedling stage; the seedling leaves were mottled and streaked with chlorotic areas. Sectors of defective tissue occurred in the older plants, of which from 5 to 10% were deficient in growth at maturity. These effects were accentuated by the heavier doses of X-rays. Plants grown from the untreated control samples exhibited the uniform growth habit characteristic of inbred lines and hybrids.

Plants that were mottled in the seedling stage had three distinct types of visible sectors in the older leaves of the nearly mature plants which were readily classified as (1) chlorophyll deficiencies, (2) morphological anomalies, including twisted, crinkled, diminutive, or otherwise deformed leaves, and (3) dead tissue, which often resulted in a longitudinal slitting of the leaves. The observed

² For additional details concerning the conduct of the Biological experiments, see R. H. Draeger and Shields Warren. *U. S. Nav. med. Bull.*, 1947, 47, 219-225.

frequencies of these types of sectors in the Bikini A and 15,000-r cultures were as follows:

The total number of plants examined was 191 from the Bikini A culture and 93 from the culture given 15,000 r

Sample	Chlorophyll deficiencies	Morphological abnormalities	Dead tissue	Plants examined	Sectors	Sectors per plant
15,000 r	68	22	20	249	110	0.44
Bikini A	126	19	73	320	218	0.60

There were fewer sectors in the cultures grown from bombed samples at greater distances from the target and those exposed to lower doses of X-rays.

The data on visible plant sectors were taken as the tassels emerged and the plants were approaching morphological maturity. The survey included only the leaves formed by the shoot apex after the seed germinated. The sectors that were recorded varied in length from approximately 50 mm to the entire length of the leaf and leaf sheath, and in width, ordinarily from 2 to 15 mm. The width of the sectors very rarely exceeded one-quarter of the width of the leaf, the larger sectors being found most frequently in the larger leaves in the region of the functional ear shoot. The prevalence of relatively small sectors in the nearly mature plant may have been due either to delayed action of the radiation or to the persistence in the region of the shoot apex of cell initials that were present in the seed. In the cytological studies of chromosomal aberrations, the sectors which were detected in the tassels ordinarily affected less than one-fifth of the tassel branches and a corresponding portion of the main spike. These tassel sectors were comparable in size to those present in the upper leaves.

There were pronounced differences in the relative frequency of the different kinds of sectors affecting the leaves in the bombed and X-rayed samples: morphological abnormalities occurred with about the same frequency, but chlorophyll deficient sectors and sectors of dead tissue were relatively much more frequent in the bombed sample than in the X-rayed sample. The cause of this selective action of the radiations from the bomb is not known.

The cytological determination of the frequency of tassel branches with visibly unaltered or normal (N) chromosomes and altered or abnormal (Abn) chromosomes involving reciprocal translocations (T), inversions (I), and deletions (D) was made at the pachytene and later stages of the first meiotic division in the microsporocytes of unselected plants of the 15,000-r and Bikini A samples. The data below were obtained from acetocarmine smears

of X-rays. Reciprocal translocation was the most prevalent type of induced chromosomal alteration, the total number observed being 5 times the number of deletions and inversions.

The same kinds of visible chromosomal alterations were induced by the atomic bomb and X-ray treatment. A somewhat higher frequency of alterations was observed at the pachytene and diakinesis stages in the X-rayed sample given 15,000 r than in the Bikini A sample; otherwise, the observed frequencies and kinds of cytological effects were very similar. Identical types of translocations, inversions, and deletions were observed with essentially the same relative frequency in the plants grown from the bombed and X-rayed seed.

The various types of observed chromosomal alterations induced by the radiations in these experiments are known to cause partial sterility. Thus, it was possible to determine their frequency of transmission simply by inspection of the pollen in the progeny of the irradiated plants. However, the different kinds of chromosomal alterations observed cytologically in these experiments could not be identified merely by looking at the pollen. For an analysis of transmission frequencies the plants in which chromosomal alterations occurred were outcrossed to untreated or very lightly treated plants. The frequency of plants in the F_1 progenies from the Bikini A and 15,000-r samples which exhibited pollen abortion was as follows:

	Plants examined	Plants with abnormal pollen	Per cent
15,000 r	769	56	7.3
Bikini A	870	60	6.9

In both series approximately 50% pollen abortion characterized most of the plants classed as having abnormal pollen; a few plants in both series had somewhat less than 50%, and a few had somewhat more than 50% of abnormal pollen. The data included pollen examinations

Sample	Pachytene			Diakinesis			Anaphase			Type of abnormality		
	N	Abn	% Abn	N	Abn	% Abn	N	Abn	% Abn	T	I	D
15,000 r	184	69	37.5	340	84	24.7	374	2	0.6	44	8	7
Bikini A	437	98	22.4	721	100	13.8	387	3	0.8	61	15	13

prepared from samples including about one-third of the lateral tassel branches of individual plants, the remainder of the tassel being left for pollen analysis.³

³ The results of the pollen analysis of these and other plants grown from the Bikini and X-rayed samples of seed will be published by E. G. Anderson and collaborators.

of 24 progenies in the X-rayed series and 41 in the bombed series.

It may be concluded from these experiments that, with respect to the kinds and frequencies of induced chromosomal alterations, the radiations from the atomic bomb produced effects in corn comparable to those induced by

exposure to approximately 15,000 r of X-rays. Both sources of ionizing radiations produced similar phenotypic effects in the plants grown from the irradiated seed, but the bomb produced relatively more chlorophyll deficiencies and dead tissue occurring as sectors than did the treatments with X-rays.

Crystalline Human Myoglobin: Some Physicochemical Properties and Chemical Composition

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Most of the researches on myoglobin refer to the horse (2, 3, 4, 8), the ox (2, 6), and the pig (5). In 1947 the writer (7) succeeded in obtaining from human skeletal muscles pure crystallized myoglobin (1-2 gr), utilizing a procedure previously described for animal myoglobin (6).

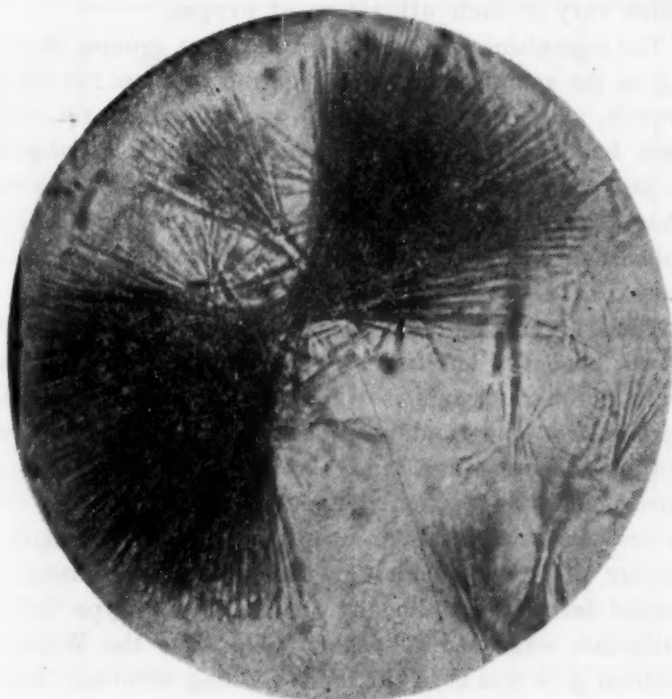


FIG. 1. Crystals of myoglobin prepared from human skeletal muscle ($\times 370$).

Human myoglobin crystals consist of long, very thin needles, tied together in subparallel bundles or in radiated, fibrous spheroidal masses (Fig. 1). The lengthening of the crystals is negative, parallel to α . Extinction is at right angles.

Crystals of metmyoglobin are clearly double-refracting, and they show an evident pleochroism with α' of a reddish-brown color parallel to the lengthening and γ' of a pale yellow color perpendicular to the lengthening; the refractive index is greater than 1.514. The iron content is 0.34%, the prosthetic group is probably the same as for hemoglobin, and the N content is 16.5%.

Spectrophotometric determinations gave maxima of 5,815 Å and 5,426 Å for the α and β absorption bands of oxymyoglobin, respectively.

The ratio between the absorption coefficients at the two

maxima for myoglobin is different from that for hemoglobin. Myoglobin is comparatively stable in an alkaline medium. The formation of hemochromogen in alkaline reducing solutions may be followed spectrophotometrically. While in 0.4 N NaOH human oxyhemoglobin is rapidly transformed to hemochromogen; the oxymyoglobin still presents the two typical α and β bands

TABLE 1

	Hemo- globin (mg)	Nitrogen	
		Myo- globin (mg)	Hemo- globin (%)
Amide N	1.79	1.95	5.86
Humine N	1.20	1.38	3.93
Cystine N	0.153	0.138	0.50
Arginine N	2.40	1.18	7.86
Histidine N	4.08	4.10	13.37
Lysine N	2.85	3.88	9.34
Filtrate NH_2 N (monoamino acids)	16.63	15.32	54.52
Filtrate non- NH_2 N (imino acids + $\frac{1}{2}$ N tryptophane)	1.26	1.50	4.13
Total N recovered	30.36	29.44	99.55

of oxymyoglobin. To obtain, in this case, hemochromogen from myoglobin, the strength of the NaOH solution has to be increased to 3 N. Myoglobins from different animals (horse, ox) behave differently toward alkali—another distinguishing feature between myoglobin and hemoglobin which is, very probably, due to the chemically different composition of the two globins.

Chemical determinations carried out with myo- and hemoglobin emphasize this difference. The nitrogen distribution and the amino acid composition have been determined on 184 mg of pure crystallized human myoglobin and 186 mg of human hemoglobin prepared in the microcrystallized form (Drabkin) by a micromodification (3) of the Van Slyke procedure (10). The nitrogen distribution in human hemoglobin and myoglobin is shown in Table 1.

TABLE 2

Amino acids	Hemoglobin	Myoglobin
Cystine	0.71	0.65
Arginine	4.00	1.98
Histidine	8.09	8.22
Lysine	7.98	11.00

In Table 2, percentages of some amino acids expressed as g% of the total amount of protein are given for both proteins.

These results represent the first contribution to the knowledge of the chemical constitution of human myoglobin. As may be seen from the analytical data (Tables 1 and 2), the chemical composition of human myoglobin is different from that of hemoglobin. The most conspicuous differences are observed in the arginine and lysine content and also in the monoamino acids.

In Table 3 the more probable distribution of the amino acids in myoglobin and hemoglobin of man and horse is

TABLE 3

	Number of amino acid molecules for 4 atoms of iron				Amount of basic amino acid for every atom of iron
	Cystine	Arginine	Histidine	Lysine	
Horse hemoglobin (4)	3	14	39	37	22
" myoglobin (4)	4	8	40	60	27
Human hemoglobin	4	16	35	37	22
" myoglobin	4	8	36	52	24

given, taking as molecular weights 68,000 and 17,000, respectively.

These data show that myoglobin of different animal species contains about half as much arginine and twice as much lysine as hemoglobin of the same animal and that the total amount of basic amino acid radicals is greater in myoglobin than in hemoglobin.

Addendum: Drabkin (1) and Theorell (9) recently mention having crystallized human myoglobin from cardiac muscle, but the writer has not yet seen these articles.

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Differential Effects of 2,4-D on Aerobic, Anaerobic, and Facultative Anaerobic Microorganisms

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2,4-Dichlorophenoxyacetic acid (2,4-D) is recognized biologically as an auxin (plant hormone) or growth-regulating substance. It is well known that 2,4-D has a selective activity on the growth rate of certain plants. The mode of action of the auxin is still a matter of conjecture, but several workers indicate that 2,4-D is involved in some way in the process of plant respiration (1, 6). Hsueh and Lou (3) developed this idea more fully in their experiments with germinating rice and barley seeds, which they treated with various concentrations

of 2,4-D before allowing them to germinate under aerobic and anaerobic conditions. The germination of barley, a typical aerobic seed, was entirely inhibited, whereas that of rice, a seed known to be able to germinate anaerobically, was only partially inhibited. The results of their experiments seemed to indicate that the rate of germination of the treated barley seeds closely paralleled that of the untreated barley seeds which were grown in an anaerobic atmosphere. It appeared as if oxygen were no longer available to the treated seeds.

That 2,4-D can display bacteriostatic and bacteriocidal properties has been shown by Stevenson and Mitchel (5) and Lewis and Hamner (4). Dubos (2) observed that a number of synthetic, unsaturated, ring-containing acids, including 2,4-D, endowed with auxin activity exerted a bacteriostatic effect on the growth of certain microorganisms. However, no correlation has been made between the effects of 2,4-D on bacteria with respect to the oxygen requirements of bacteria.

The purpose of this report is to demonstrate the effects of different concentrations of 2,4-D on those organisms which vary in their utilization of oxygen.

The organisms were divided into three groups, depending on the amount of oxygen required by them for normal growth. Among the aerobes, or those bacteria which must have free oxygen, *Rhizobium trifolii*, *R. phaseoli*, *R. japonicum*, and *Azotobacter chroococcus* were selected. These were obtained from the American Type Culture Collection at Georgetown University. The anaerobes, those organisms which will grow only when oxygen is excluded, were represented by *Clostridium welchii*, *Cl. tetani*, and *Cl. botulinum*. The facultative anaerobes, those aerobic organisms which can grow anaerobically, were selected at random and included *Escherichia coli*, *Staphylococcus albus*, and *Candida albicans*. The anaerobes and the facultative anaerobes were obtained from clinical material in Duke Hospital. It was necessary to employ different media for the various organisms. A special formula supplied by the American Type Culture Collection was used for *R. trifolii*, while the Waksman medium #79 was used for the remaining aerobes. Brain-heart infusion agar was used for the anaerobic and facultative anaerobic organisms. All of the media employed were adjusted to a pH of 7.4.

Sodium 2,4-dichlorophenoxyacetate, obtained from the J. T. Baker Chemical Company, was used throughout the present study. Solutions of the 2,4-D were prepared and diluted with distilled water to concentrations of 5, 1, 0.1, 0.01, and 0.001% and autoclaved for 15 min. at 18 lbs pressure. Varying amounts of these solutions were measured into a series of tubes of the agars used to give a final volume of 5 cc of agar-2,4-D solution/tube. The final concentrations of 2,4-D, after taking into account the dilution factor of the agar, amounted to 2, 1, 0.2, 0.02, 0.002, and 0.0002%/5 cc of diluent. The number of grams of 2,4-D/5 cc of agar were 0.1, 0.5, 0.25, 0.001, 0.0001, and 0.00001. The agar containing the auxin was poured into level Petri dishes which contained a base of approximately 10-15 cc of the corresponding type of agar.

The organisms were subcultured for 24 hrs on agar slants, which were then washed with a measured quantity of 0.85% saline and streaked with a wire loop on the prepared plates. Each organism was tested against the 6 concentrations of 2,4-D and on control plates containing no 2,4-D. The aerobes were left at room temperature, while the facultative anaerobes were incubated at 37.5° C. The anaerobes were incubated at 37.5° C in Brewer anaerobe jars. Since control plates were em-

a difference of 1 plus in any two recordings should not be interpreted as too significant.

In general, all four of the aerobes tested were inhibited by 2,4-D, particularly in the higher concentrations. At the 48- and 72-hr readings it appeared as if the lower concentrations of 2,4-D increased the amount of growth. No inhibitory effects were observed with the facultative anaerobic organisms, and in the lower concentrations there was an increase in the amount of

TABLE 1
COMPARISON OF AMOUNT OF GROWTH OF MICROORGANISMS ON MEDIA TREATED WITH 2,4-D

	Organism	Time of reading (hrs)	Control	Amount of 2,4-D/5 cc of agar expressed in per cent and grams					
				2% (0.1 gm)	1% (0.05 gm)	0.2% (0.025 gm)	0.02% (0.001 gm)	0.002% (0.0001 gm)	0.0002% (0.00001 gm)
Aerobic organisms	<i>R. trifolii</i>	24	4	0	1	3	4	4	4
		48	4	0	2	4	5	5	5
		72	4	1	4	2	5	6	6
	<i>R. phaseoli</i>	24	0	0	0	0	0	0	0
		48	4	0	0	0	0	0	3
		72	4	0	0	1	3	4	4
	<i>R. japonicum</i>	24	0	0	0	0	0	0	0
		48	4	0	0	0	0	0	0
		72	4	0	0	0	1	0 (1)	0 (1)
	<i>A. chroococcus</i>	24	4	0	0	0	0	0	2
		48	4	4	4	4	4	4	4
		72	4	4	4	4	4	4	4
Facultative anaerobic organisms	<i>E. coli</i>	24	4	4	4	4	5	4	4
		48	4	4	4	5	5	5	4
		72	4	4	4	5	5	5	4
	<i>Staph. albus</i>	24	4	4	5	6	6	6	5
		48	4	4	5	6	6	6	5
		72	4	5	5	6	6	5	5
	<i>C. albicans</i>	24	4	4	4	5	5	4	4
		48	4	4	4	5	5	5	4
		72	4	4	4	5	5	5	4
Anaerobic organisms	<i>Cl. welchii</i>	24	4	2	3	3	2	4	3
		48	4	3	3	3	1	4	4
		72	4	4	4	4	2	4	4
	<i>Cl. botulinum</i>	24	4	1	1	3	3	3	3
		48	4	3	1	3	2	4	3
		72	4	3	2	3	2	4	2
	<i>Cl. tetani</i>	24	4	4	5	4	5	4	4
		48	4	3	5	4	2	4	2
		72	4	3	5	4	4	4	4

Key: 0 = no growth, 0 (1) = slight growth, 1 to 2 = poor growth, 3 = good growth, 4 = growth on control plate, 5 to 6 = growth exceeding that on control plates.

employed for each organism, the differences in the temperature do not affect the interpretation of the results obtained. The amount of growth was read at 24-, 48-, and 72-hr intervals. The control of each organism was considered as 4 plus growth, and the remaining plates were compared with the controls. The results are shown in Table 1. Since a human error may enter at this point,

growth over that on the control plates. The response of *Cl. tetani* resembled that of the facultative anaerobes in that there was an increase in growth with the lower concentrations and no apparent inhibition at higher concentrations. *Cl. welchii* and *Cl. botulinum*, however, vary in their response to 2,4-D, and it is difficult to formulate definite conclusions. There is some slight

inhibition of these two organisms with the highest concentrations, but this result is insignificant when compared with the response of the aerobes. The repeated exposure of these latter clostridia to atmospheric oxygen at the three periods of recording may have affected their rate of metabolism in sufficient degree to cause the irregular effects produced.

From the data accumulated it appears that those organisms which require free oxygen for respiration are "smothered" by 2,4-D. They react in a manner similar to the germinating barley seeds as reported by Hsueh and Lou. Those organisms capable of anaerobic respiration only are not affected to any significant degree by 2,4-D.

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The Relative Sensitivities of Bacterial Viruses to Intense Sonic Vibration¹

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It was thought that the multiplication of bacterial viruses might be followed up to the moment of natural lysis by sonically disintegrating infected bacteria at various times after infection. An electron microscope study of the debris might then reveal the various morphological stages in virus proliferation, while counts of infectious particles would permit estimation of the rate of appearance of mature particles. However, preliminary studies of T2 virus, which, because of its easily recognizable tadpole shape, would be ideal for this purpose, showed that it is even more rapidly disintegrated by sonic vibration than the host cells and, therefore, would be unsuited for the proposed investigation (1). In an attempt to find suitably resistant viruses we have followed the sonic

¹This work was supported by Contract N6-ori-168, T.O. II between the Navy Department and the Trustees of the University of Pennsylvania and by a grant from the Raytheon Manufacturing Company.

In the oscillator (Type R-22-1) used for this work the vibrating system consists of a stainless-steel diaphragm which forms the base of the specimen cup and laminated nickel strips, the ends of which are attached to the diaphragm. The system is caused to vibrate by oscillating magnetic fields set up by a solenoid surrounding the nickel strips and on which the cup rests. A power supply operating on 110-volt, 60-cycle current and tuned to resonate with the mechanical system provides the driving power which is transmitted to the sample by the vibrating diaphragm. Cooling water flows through a jacket surrounding the cup and sprays over the nickel strips within the solenoid. The average temperature of the specimen is thus held to within a few degrees of that of the cooling water, even during cavitation of the liquid.

inactivation of each of a set of 7 viruses (T1-T7) (5) active on *E. coli*, strain B. Since an interesting correlation between structure and sensitivity was obtained, we are recording the results here.

Forty-cc filtered samples of each of the bacteriophages were treated separately in the water-cooled cylindrical cup of a magnetostriction sonic oscillator manufactured by the Raytheon Manufacturing Company. Samples were removed at intervals and, together with the untreated control, were assayed for virus activity by the plaque count method. Samples of the host bacteria were treated in an analogous manner and their survivals determined by colony counts.

TABLE 1

PERCENTAGE SURVIVAL OF VARIOUS BACTERIOPHAGES AND OF THEIR HOST, *E. coli* STRAIN B, AFTER EXPOSURE TO INTENSE SONIC VIBRATION

Length of exposure (min)	Bacteriophage							<i>E. coli</i> Strain B
	T1	T2	T3	T4	T5	T6	T7	
1	92	73	70	50	30	100	80
5	34	1.8	80	0.8	1.6	0.9	60	18
10	30	.07	80	0.009	0.07	0.008	40	1
30	10	..	40	12	0.016
60	1	..	0	1.1

In Table 1 are given the results of a typical series of experiments. It is seen that viruses T2, T4, T5, and T6 are more rapidly inactivated than the host bacteria, while the remaining three viruses, T1, T3, and T7, are remarkably resistant to sonic vibration.

These results are interesting in relation to the morphologies of these viruses as seen in the electron microscope (2). The resistant viruses T3 and T7 appear to be small spheres 450 A in diameter (3, 4) while T1 is a similar small sphere but with a faint, 1,200-A-long tail attached (6). In contrast, the vibration-sensitive viruses T2, T4, and T6 are relatively large, tadpole-shaped structures with frequently pointed heads 600 x 800 A, consisting of an internal structure and surrounding membrane to which a well-defined tail approximately 1,000 A long is attached (2). Likewise, the sensitive virus T5 has a large, round head about 900 A in diameter, also consisting of a membrane surrounding internal structures and with a faint tail some 1,700 A long attached (2). It seems likely that the sensitive viruses with their relatively large and complex structures are mechanically disintegrated by intense vibration, while the small, compact viruses are relatively resistant to the shearing forces existing during cavitation of the liquid in which they are suspended.

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IN THE LABORATORY

Three-dimensional Modeling of Cyclones in Elementary Meteorology

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Students in elementary meteorology have more or less trouble in visualizing wave cyclones in three dimensions. For the past 6 years the writer has found helpful a laboratory exercise based on the use of a sheet of plasticine as the boundary surface between the air masses involved. In addition to the plasticine sheet ($\frac{1}{4} \times 10 \times 16$ is a convenient size), each student needs some small blocks of plasticine to prop up the main sheet, a knife, a few tack pins with paper arrows colored to represent the cold and warm winds, a sheet of corrugated cardboard for the ground surface, and chalk to draw successive positions of the fronts on the "ground."

Given this material, the student proceeds to develop the successive stages in the standard Bjerknes wave cyclone "model." After the plasticine has been blocked up at a reasonable angle for a straight stationary front, the wave can be initiated and excess plasticine trimmed out so that the boundary sheet is in continuous contact with the ground. As the warm sector enlarges, additional trimming is done. When the occlusion stage is reached, the plasticine is split a sufficient distance up from the ground junction of the warm and cold fronts and one side tucked under. Thus, from the same cut the plasticine can be shaped to show either a warm or cold front type occlusion. Experience has shown that, once a student has gone through this entire sequence himself, he understands the structure of wave cyclones far better than if he were to rely on the standard cross sections alone.

Isolation of Crystalline Desoxyribonuclease From Beef Pancreas¹

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A crystalline protein having a powerful desoxyribonuclease activity has been isolated from fresh beef pancreas by the method outlined below. Specific enzymatic activity of the protein is not diminished on recrystallization.

(1) *Preliminary purification by a modified McCarty's procedure* (2). An acid extract of ground beef pancreas, prepared according to the method of Kunitz and Northrop

(1), is brought to 0.2 saturation of ammonium sulfate (114 gm of the salt/liter of extract). The solution is filtered with suction on Eaton and Dikeman No. 642 paper with the aid of 10 gm of Celite 503 (Johns-Manville Corporation) and 10 gm of standard supercel/liter of solution. The clear filtrate is then brought to 0.4 saturation of ammonium sulfate (121 gm/liter) and re-filtered with suction, with the aid of 3 gm of Celite 503/liter, on Eaton and Dikeman No. 612 paper. The filtrate can be utilized for the preparation of chymotrypsinogen, trypsin, and ribonuclease. The residue, including the Celite, is suspended in 5 times its weight of water. The suspension is brought to 0.3 saturation of ammonium sulfate (176 gm/liter of water) and re-filtered with suction, the filtrate then being discarded.

(2) *Incubation at 37° C followed by fractionation with ammonium sulfate.* The residue is suspended in 10 times its weight of water, and the suspension is brought to 0.15 saturation of ammonium sulfate (83.7 gm of salt/liter of water). The solution is titrated with about 2 ml of 5 N H₂SO₄/liter to pH 3.2 (glass electrode), heated to 37° C, and incubated for 1 hr at that temperature, after which it is cooled to about 20° C and filtered with suction with the aid of an additional 5 gm of Celite/liter of suspension. The residue is discarded.

The filtrate is titrated to pH 5.3 with 5 N NaOH (about 2 ml/liter) and brought to 0.5 saturation of ammonium sulfate (220 gm/liter). The precipitate formed, designated as "0.5 s.a.s. precipitate," is filtered with suction with the aid of 5 gm of Celite/liter of solution.

The clear filtrate is titrated with a few drops of 5 N H₂SO₄ to pH 4.0 (green to bromocresol green on test plate) and brought to 0.7 saturation of ammonium sulfate (135 gm/liter). The light precipitate formed, designated as "0.7 s.a.s. precipitate," is filtered with the aid of 2 gm of standard supercel/liter. The filtrate is discarded.

The "0.5 s.a.s. precipitate" (including the Celite) is then resuspended in 10 times its weight of water and operation 2, including the incubation at 37° C, is repeated several times until no appreciable "0.7 s.a.s. precipitate" is formed. The combined "0.7 s.a.s. precipitate" is suspended in about 10 times its weight of water and filtered with suction. The supercel residue is washed several times with water until the washing is water clear.

(3) *Fractionation with ethyl alcohol.* The combined filtrate and washings are diluted with water to a concentration of about 10 mg of protein/ml.² The pH of the solution is adjusted with 5 N H₂SO₄ to about 3.8, and 2 ml of saturated ammonium sulfate is added/100 ml of solution, which is cooled in an ice-salt bath to about 2° C. One-quarter of its volume of cold 95% alcohol is added

¹The writer appreciates greatly the very helpful cooperation of Maelyn McCarty, at whose suggestion this work was initiated.

²The approximate concentration of protein can be determined spectrophotometrically at 280 mμ, the optical density being about 1.2/mg of protein/ml.

slowly with stirring in order to keep the temperature of the solution below 5° C. After the mixture has been stored for 24 hrs at about 5° C it is centrifuged at the same temperature. The residue is discarded, or saved for partial recovery of active material, while the clear supernatant solution is left at about -10° C for 24 hrs. It is centrifuged at the same temperature. The precipitate, called the "second alcohol precipitate," contains most of the enzymatic activity of the original "0.7 s.a.s. fractions."

(4) *Crystallization.* The "second alcohol precipitate" is dissolved in about 10 times its volume of water, after which it is brought to 0.38 saturation by addition of 60 ml of saturated ammonium sulfate/100 ml of solution.

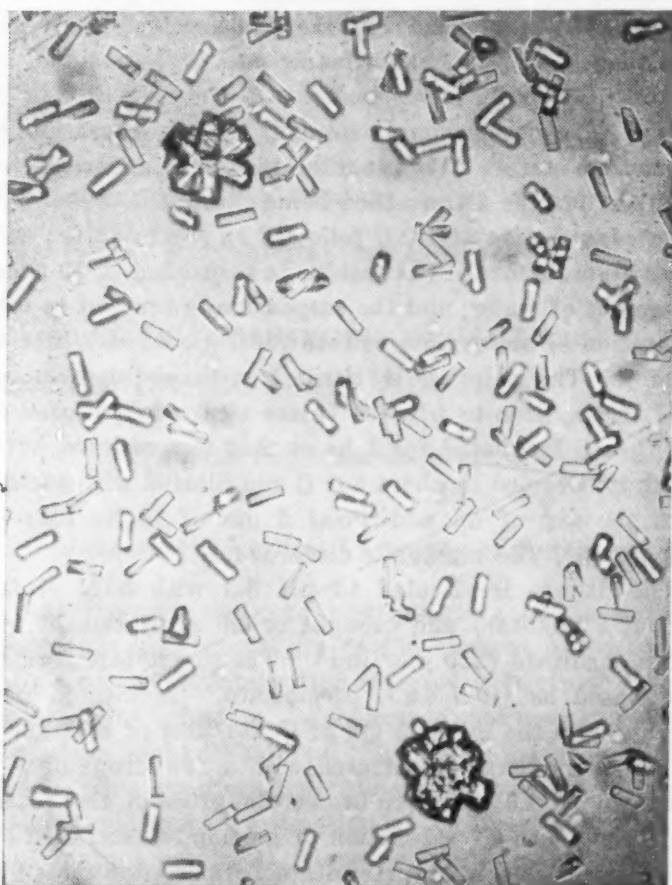


FIG. 1. Crystals of desoxyribonuclease ($\times 234$).

The precipitate formed is filtered with suction on hardened paper. It is then suspended in 3 times its weight of water and dissolved with the aid of several drops of 0.2 or 0.5 N NaOH. The solution, if turbid, is filtered clear on a small, folded Whatman No. 3 paper. The pH of the filtrate is adjusted to about 2.8 (glass electrode) with several drops of 0.2 N H_2SO_4 . The solution is seeded and left at 5° C overnight and then at about 20° C for 6-8 hrs. Crystals appear at room temperature (Fig. 1).

(5) *Recrystallization.* The suspension of crystals is centrifuged. The sedimented crystals are suspended in about 3 volumes of 0.02 saturated ammonium sulfate solution and dissolved with the aid of a few drops of 0.2 N NaOH at a pH of about 4.4. The solution, if turbid, is filtered, titrated to pH 2.8, and then left at 20° C. Crystallization proceeds rapidly. The crystals, filtered with suction on hardened paper, are washed, first with ice-cold acidified 30% alcohol (1 drop 5 N H_2SO_4 /100

ml), then with cold acetone, and dried at room temperature for several hours. The dry preparation is stored at about 5° C. The supernatant solution may yield more crystals on reprecipitation with ammonium sulfate; the precipitate is treated as described in step 4.

The properties of the crystalline material are now being investigated.

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An Improved Method for Mounting Small Insects

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In the course of several years work with *Phlebotomus* sand flies we have been faced with the necessity of devising a rapid method of making permanent slide mounts of these insects which will show the delicate internal structures without shrinkage or distortion. We have tried numerous formulas of the Gater's medium type, but even when carefully ringed, they have failed uniformly in less than a year under our tropical conditions. The usual methods involving dehydration with alcohols of increasing concentration, xylol or clove oil and balsam are tedious and almost invariably result in shrinkage of the delicate spermathecae. Furthermore, treatment with alcohol and xylol tends to make the specimens very brittle. Lutz (1) pointed out the advantages of pure phenol as a clarifier and dehydrator, and O. Mangabeira told us of his use of it in preliminary identification of large numbers of sand flies. After a number of trials we have devised the following procedure, which has given excellent results with *Phlebotomus*, at least and should be adaptable to other small and delicate insects:

(1) Treat with strong KOH (10-20%). The specimens may be very briefly boiled, heated in a water bath, or left for several hours in the cold solution, the point being to macerate thoroughly and remove all tissue, leaving only the sclerotized structures. We find it best to remove the wings and separate the head and abdomen from the thorax before treatment with KOH. The wings are not treated with KOH but placed in the stain, where they await the rest of the specimen. Material that has been preserved for some years in alcohol is resistant to treatment with KOH, needs more prolonged treatment than do freshly caught specimens, and never makes satisfactory mounts.

(2) Rinse in water. We find that prolonged washing or acidification is unnecessary, but all strands and bits of tissue must be removed from the specimen, as they take the stain very heavily and shrink badly in the final resinous medium, obscuring and distorting the other structures. We do the rinsing in a hollow ground slide under a binocular microscope, where the specimen may be rolled about and squeezed, the elasticity of the integument al-

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wing the head and abdomen to be "pumped" like a rubber bulb, thus expelling any free bits of tissue within.

(3) Place in stain. The stain is made by dissolving acid fuchsin in pure phenol. Acid fuchsin is only sparingly soluble in phenol, so that a saturated solution is clear dark pink. For use, dilute the concentrated stain with at least an equal quantity of phenol in a hollow ground slide and stain for about 20 min. Should the specimen be overstained, destaining may be done in phenol to which a little KOH has been added.

(4) Rinse off the superfluous stain in pure phenol. The specimens may be left in pure phenol at least several hours without destaining, though too prolonged a stay in phenol will destain. The phenol used must be fresh and clear. We allow phenol crystals to liquefy in an open dish, after which they are kept covered. Old phenol will not make a satisfactory stain, and stained specimens will destain rapidly when placed in it.

(5) Mount. Since xylol balsam has a tendency to take up water under tropical conditions and hardens too rapidly, we use balsam or copal dissolved in pure phenol. The Canada balsam-phenol mixture darkens rather rapidly and must be made up fresh every month or so, but copal darkens much less rapidly and is equally satisfactory in other respects. In mounting, the separated head, thorax, abdomen, and wings are placed in separate small drops of phenol-copal on a small cover glass, the medium being allowed to harden a few hours or overnight. The cover slip is then turned over onto a generous drop of phenol-copal or ordinary thick balsam. This insures the speci-

mens being close to the cover slip and accessible to the oil-immersion lens. It is important that the cover slip be supported in the final mount by chips of cover slip at the corners, as shrinkage during drying will crush and distort the specimen. The final mounts must be thoroughly dried with gentle heat; otherwise, the residual phenol may crystallize out in fine needles and spoil the specimen.

In mounting the abdomens of female *Phlebotomus*, we find it necessary to proceed gradually from pure phenol to the resinous mounting medium; otherwise, the thin-walled spermathecae will collapse. This may be done by placing the abdomen under a cover slip in phenol, either supported on a flat slide or in a hollow ground slide and gradually adding thinned resinous mounting medium at one edge, withdrawing the phenol a little at a time from the opposite side with a bit of filter paper. When the medium under the cover slip has become sufficiently concentrated, the abdomen may be transferred to the inverted cover slip in a drop of medium and allowed to dry with the rest of the specimen. In processing unidentified female specimens of *Phlebotomus*, it is wise to examine the spermathecae either in phenol or in water after KOH treatment, as the spermathecae and their ducts are best seen at this stage. If the specimen is of special value, drawings should be made at this time, since, even with the most painstaking care, shrinkage and collapse may occur in mounting.

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Book Reviews

Plants and environment: a textbook of plant autecology.
R. F. Daubenmire. New York: John Wiley; London: Chapman & Hall, 1947. Pp. xii + 424. (Illustrated.) \$4.50.

Prof. Daubenmire believes that course work in ecology should be preceded by the study of plant morphology, taxonomy, physiology, and chemistry. He also believes that the study of vegetation should not be undertaken until the student has a grasp of the numerous and often complex influences which affect the individual plant, and of the attendant responses of plant life to such influences. Thus, his approach is analytical and deductive.

For the purpose of exposition he breaks down environment into 7 "factors"—soil, water, temperature, light, atmospheric and biotic factors, and fire—and devotes a generous chapter to each. The two concluding chapters deal, respectively, with "The Environmental Complex" and "Ecologic Adaptation and Evolution." A list of 612 references in English and a detailed index are appended.

Throughout the book there is a beautiful consistency of style and organization. Both are lucid, logical, economical, and yet thorough. The illustrations, which are

well chosen, are in large part original and bespeak the author's long discipline in the field. These merits, together with the sound critical scholarship which the book displays, reflect honor both upon the author and upon the fine American ecological teaching tradition of which he is a product. Happily, too, *Plants and environment* tends to round out, rather than displace in any measure, the small but vigorous teaching literature on ecology which is available to students in this country.

By the canons of criticism, if an author accomplishes what he sets out to do, and does it well, there is nothing more to say. Yet I do not believe the book would have suffered in any respect if Prof. Daubenmire had given some play to his "conception of the synthetic nature" of ecology and to his belief in the fundamental importance of the "holistic outlook." He does himself less than justice when he calls the environment the *sum* of all its factors. He knows, and later makes clear, that the relationship is not merely additive.

In short, the ultimate business of all ecology is the inseparable relationship between process and form. It seems scarcely sufficient to mention the application of Le Chatelier's theorem. The fundamental physical con-

cept from which it derives ought to be made clear to every student of biological processes. Nor should it be necessary to become involved in "the several conflicting philosophies of plant sociology" before one can show that the living community has the attribute of form by virtue of the processes of which it is an expression.

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The corrosion handbook. Herbert H. Uhlig. (Ed.) New York: John Wiley; London: Chapman & Hall, 1948. Pp. xxxiii + 1188. (Illustrated.) \$12.00.

This volume was prepared as a project of the Corrosion Division of the Electrochemical Society. Approximately 100 contributors supplied 142 articles which make up the book. These articles have been grouped into 9 sections: Corrosion Theory; Corrosion in Liquid Media, the Atmosphere, and Gases; Special Topics in Corrosion; High-Temperature Corrosion; High-Temperature Resistant Materials; Chemical Resistant Materials; Corrosion Protection; Corrosion Testing; and Miscellaneous Information.

As the title implies, the principal purpose of this book is to provide a single source of information, in terms of data and observations, concerning corrosive effects of a wide variety of media on many substances, metallic and nonmetallic. The authors chosen to present this material were well qualified on the basis of their interest or direct efforts in the particular areas covered. The purpose has been served directly in most instances or through references to the original literature. The information given necessarily lags behind the research in the field, but this does not detract from its usefulness.

A number of widely used experimental methods for measuring corrosion rates in the laboratory and in the field are described in some detail. Brief descriptions of various general techniques which might gainfully be applied to corrosion research, e.g. microscopy, X-ray diffraction, electron diffraction, wetting, adsorption, and others, could have been added profitably.

Theoretical aspects of corrosion as such are treated only briefly in about the first 40 pages, but considerable discussion of fundamentals may be found in many of the individual articles. On reading the book, the newcomer to the field will have no difficulty in determining the prevailing opinion on theories of corrosion mechanism, corrosion inhibition, passivity, etc. At the same time there are sufficient expressions of conflicting opinion to indicate that much is still improperly understood. It follows, then, that this book might well stimulate research in corrosion.

The physical make-up of the book is satisfactory, and there are many useful photographs, figures, and references to the original literature. A badly needed glossary of terms is included, and the index, an important item in such a book, is adequate. The book will serve very well the engineer and the scientist interested in corrosion.

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Scientific Book Register

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